

April 29, 1959

Dr. Joseph Lein, Director  
Microbiological Research  
Bristol Laboratories Inc.  
Syracuse 1, New York

Dear Joe:

To yours of the 24th.

Thank you for renewing your invitation but while we have sharply curtailed our trip to Europe, we still have to be away most of May and June. I know you are proud of your new labs and will be more so of what comes out of them.

As to penicillins, it is hard to suggest anything that is not obvious. You will be wanting to screen as quickly as possible for resistance to penicillinase and it would be difficult to predict in advance what side groups would do this. The models suggest that it might just be possible to protect the lactam from approaching the hydrolytic enzyme by substituting some very bulky groups on the free amino position. Alternatively one might put on some highly charged residues. Of course what these will do to the antibacterial activity of the penicillin remains to be found.

Anything further on the preparation of phosphate-substituted metabolites? My own hunch for the cancer problem is very strongly in the direction of an analogue of RNA from tumor cells and the main obstacle to testing this out may be achieving its penetration into the target cells.

I guess S.R.I. has been dragging its feet on our joint proposal but I think they have had some personnel rearrangements that might account for it. I do hope they come through.

Yours as ever,

Joshua Lederberg